A conversation with Miguel Barbosa

By Steve Edelson, Executive Editor of New Media

At least three big biopharmas are rethinking how to attack inflammatory bowel disease. The common thread is large-scale efforts to shed light on the underpinnings of the disease.

SciBX spoke with Miguel Barbosa, VP and head of immunology research and scientific partnership strategy at Janssen Research & Development LLC, about the IBD space.

Barbosa thinks IBD—like some other diseases—requires a different drug discovery approach from the historical tack of one molecule for one target. To change direction, he said, will require a combination of external collaboration and fresh thinking about navigating clinical and regulatory development.

In July 2013, the Janssen unit of **Johnson & Johnson** partnered with the **Icahn School of Medicine at Mount Sinai** to investigate triggers of IBD, identify new opportunities for therapeutic intervention and create diagnostics for use as therapeutics or predictive biomarkers. The deal combines Janssen's R&D capabilities with Mount Sinai's expertise in computational biology and clinical and translational research.

Other companies have also looked to academia for IBD deals this year. **Amgen Inc.** partnered with **Massachusetts General Hospital** and the **Broad Institute of MIT and Harvard** to find new IBD targets. The collaborators will use materials from the Prospective Registry in IBD Study at MGH (PRISM), which stores pre- and post-treatment biopsy and fecal samples from several hundred patients with IBD.

The partners are taking an unbiased approach, and Amgen has said the ideal result from the self-described fishing expedition would be a druggable protein—encoded by an IBD risk-reducing variant—that has lower function than the wild-type protein.¹

Pfizer Inc. is the most recent entrant, with a pair of August partnerships. First, the pharma partnered with **23andMe Inc.** to explore the genetic factors associated with the onset, progression and severity of IBD and to identify patients who are likely to respond to treatments.

23andMe will recruit about 10,000 U.S. patients with Crohn's disease or ulcerative colitis and will supply them with 23andMe's Personal

Genome Service at no cost. Pfizer wants to use the resulting genetic information in part to identify patients who are more likely to respond to treatments. Financial terms were not disclosed.

About a week later, Pfizer partnered with the **Crohn's & Colitis Foundation of America** to fund up to four academic projects focused on developing small molecules to treat Crohn's disease and ulcerative colitis.

SciBX's interview with Barbosa follows.

SciBX: Part of your operating hypothesis is that the easy-to-find drug targets are already taken. What does that mean for how you think about treating IBD and diseases in general?

Miguel Barbosa: We have to acknowledge diseases are very complex biological systems that more often than not cannot be reduced to a single target and molecule. We have an approach that allows us to collaborate broadly with key academic labs that specialize in very specific diseases and connect us to a set of samples. Then we can use advanced computational systems to mine that data to really unearth these complex biological networks that are driving either the healthy space or are driving the pathology that is underlying disease.

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—Miguel Barbosa, Johnson & Johnson

SciBX: Janssen's deal with Icahn seems like a prime example of this strategy. How are the parties working together?

MB: We have had products make it all the way from discovery to development and are actually now on the market in the field of IBD. We share this information with our collaborator, and they share their deep understanding of the clinical aspects of the disease, and together we can mine for novel mechanisms that would allow us to discover and

develop a new generation of therapeutics addressing the remaining unmet medical need.

SciBX: What's happened in the first year of the collaboration, given the two groups are wrestling with what are likely very different datasets?

MB: We have made a significant amount of progress through the first phase, which was the integration of the datasets and the mining of those datasets. The team is beginning to probe incrementally the new mechanistic concepts that we were able to uncover through a computational analysis approach.

SciBX: Can you share any of the new concepts you've uncovered?

MB: At this time that would not be appropriate.

SciBX: How do you think Janssen's approach compares with how Amgen and Pfizer are tackling IBD via their respective deals this year?

MB: I cannot really do a compare and contrast because of course I'm not privy to the details of the Amgen partnership. I will say that when you start from the genetic makeup of the individual and look at the public literature, there is a significant number of gene associations that suggest risk in terms of potential to develop the disease. But IBD is complex because the gene itself is not sufficient to lead to the disease. There are other events that take place through other mechanisms.

[Pfizer's] collaborations make good sense for a new entrant in the IBD field as a way to leverage existing scientific and clinical networks.

The partnership we have with Icahn really allows us to mine that complex set of events that in some cases leads to triggering a full-fledged autoimmune disease such as IBD. And because of that integrated approach—together with the advanced computational tools—we are able to come up with testable concepts that look at a combination of medical events with environmental insults that ultimately are associated with the disease itself.

SciBX: If we were to chat in two or three years and look back on the programs and initiatives, what would you hope to be pointing to as a success?

MB: In that time frame I would hope that we would begin to talk about the specific mechanisms that we have in our clinical development pipeline that are looking at more complex mechanisms that are targeting multiple targets at the same time. We would be able to talk about the progression of some of these early phase projects that we are just embarking on.

One of the components that we have as part of our strategy is really to match the specific therapeutic model with a patient population we

believe would be best responders to that treatment. And that's where we apply a co-diagnostic strategy as part of the therapeutic approach. And so within that time frame we would, I hope, be talking about successes in particular in IBD.

SciBX: This idea of targeting multiple mechanisms simultaneously—are clinical developers and regulators going to have to play catch-up to get up to speed, either on new ways of running trials or new approvable endpoints?

MB: The discussions are all taking place. One of the challenges is going to be to increase the clarity of how the clinical development plan is designed as well as the regulatory path. It will vary depending on whether you have multiple compounds that are put together into one pill or a single entity that has been engineered to actually target two different molecules, for example.

SciBX: Thank you very much for your time.

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COMPANIES AND INSTITUTIONS MENTIONED

23andMe Inc., Mountain View, Calif.

Amgen Inc. (NASDAQ:AMGN), Thousand Oaks, Calif.

Broad Institute of MIT and Harvard, Cambridge, Mass.

Crohn's & Colitis Foundation of America, New York, N.Y.

Icahn School of Medicine at Mount Sinai, New York, N.Y.

Johnson & Johnson (NYSE:JNJ), New Brunswick, N.J.

Massachusetts General Hospital, Boston, Mass.

Pfizer Inc. (NYSE:PFE), New York, N.Y.